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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/671,697

09/29/2003

Jean-Yves Bonnefoy

1430-287

7814

23117

7590

09/10/2007

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EXAMINER

BASI, NIRMAL SINGH

ART UNIT

PAPER NUMBER

1646

MAIL DATE

DELIVERY MODE

09/10/2007

PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/671,697	<b>Applicant(s)</b> BONNEFOY ET AL.	
	<b>Examiner</b> Nirmal S. Basi	<b>Art Unit</b> 1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 19 June 2007.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 22-45 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 22-45 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)                                | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                       | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

## DETAILED ACTION

1. Amendment filed 6/19/07 has been entered. Applicant has amended claim 22 and added new claims 23-45. Claims 22- 45 will be examined as they pertain to the elected invention. The rejections below have been recast to address applicants amendments.

### ***Claim Rejections - 35 USC § 112, 1<sup>st</sup> Paragraph***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 22-39, 40-41, 44-45 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The amendment filed 6/19/07 introduced new matter into the claims, which is not supported by the original disclosure. The new matter pertains to the use of “**specific for binding**” or “**specific binding in the claim**.”

The specification does not support the narrower limitations of the combination of elements currently claimed i.e. an isolated antibody or an isolated antibody fragment thereof which is “**specific for binding to a polypeptide**”, “**molecule which is specific for binding**”, or “**specific binding**” The use of the

Art Unit: 1646

word "**specific**" implies a genus of antibodies that is not supported by the specification.

There is no written description in the specification for the combination of the limitations disclosed above. If Applicant feels Examiner's assessment of the new matter is in error then he/she must clearly disclose where in the specification specific support for the combination of elements currently claimed can be found. In particular applicant must point out the use of the word "specific" as it pertains to the claims.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 22-39, 40-41, 44-45 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 22, 23, 26, 29, 31, 34, 35, 36, 37, 40, and 44 are rejected as indefinite because it is not clear which antibodies would be considered "**specific**" for binding to a polypeptide comprising SEQ ID NO:9 or a polypeptide comprising SEQ ID NO:9 wherein Thr residue number 130 and Gly residue number 358 shown in SEQ ID NO:9 are replaced by Ile and Asp residues, respectively." The term "specific" for binding to a polypeptide is not defined in the specification so as to allow the metes and bounds of the claims to be determined. Antibody specificity is measured in terms of its  $K_m$  or  $K_d$  for an antigenic epitope. The region of a protein molecule to which an antibody can bind is defined as an

Art Unit: 1646

antigenic epitope". The specification does not define "specific" for binding to a polypeptide in terms of  $K_m$  or  $K_d$ . Therefore, an antibody that binds an epitope on two separate proteins, A and B, be it the same epitope or different, the antibody would be considered specific for binding to polypeptide A as well as specific for binding to polypeptide B. Therefore, in the absence of any association or dissociation constants,  $K_m$  and  $K_d$ , by which to define specific binding of an antibody to a protein, the term "specific" binding to a polypeptide is limited by the epitope to which it binds. In the rejections that follow if an antibody can bind a polypeptide it is considered specific binding.

Claims 24-25, 27-28, 30, 32-33, 41 and 45 are rejected for depending on an indefinite base claim and failing to resolve the issues raised above.

### ***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

4. Claims 22-24, 26, 27, 29-35 are rejected under 35 U.S.C. 102(e) as being anticipated by Wilson et al (US Patent 6,911,530, which is a divisional of 09/051,843 filed 10/23/96).

Art Unit: 1646

Wilson discloses a method of making an antibody and an antibody that binds to NR4 polypeptide. The NR4 polypeptide, i.e. interleukin receptor alpha chain (SEQ ID NO:4 and 2) of Wilson have 98.9% and 72.9% query match respectively, with the polypeptide of SEQ ID NO:9 of instant application (IL-13 receptor). The receptor SEQ ID NO:4 contains the Thr/Gly and Ile/Asp amino acid replacements. The NR4 polypeptide is collectively used to refer to the polypeptide of SEQ ID NO:4 and 2.

Sequence comparison of SEQ ID NOs:4 and 2 (Wilson patent) with SEQ ID NO:9 (instant application) are shown below:

## RESULT 4

US-09-688-286D-4

; Sequence 4, Application US/09688286D

; Patent No. 6911530

; GENERAL INFORMATION:

; APPLICANT: Willson, Tracey

; APPLICANT: Nicola, Nicos

; APPLICANT: Hilton, Douglas

; APPLICANT: Metcalf, Donald

; APPLICANT: Zhang, Jian

; TITLE OF INVENTION: A novel haemopoietin receptor and genetic sequences encoding same

; FILE REFERENCE: 23199-215

; CURRENT APPLICATION NUMBER: US/09/688,286D

; CURRENT FILING DATE: 2003-07-10

; PRIOR APPLICATION NUMBER: AU PN6135

; PRIOR FILING DATE: 1995-10-23

; PRIOR APPLICATION NUMBER: AU PN7276

; PRIOR FILING DATE: 1995-12-22

; PRIOR APPLICATION NUMBER: AU PP2208

; PRIOR FILING DATE: 1996-09-09

; NUMBER OF SEQ ID NOS: 12

; SOFTWARE: PatentIn version 3.1

; SEQ ID NO 4

; LENGTH: 426

; TYPE: PRT

; ORGANISM: human

US-09-688-286D-4

Query Match 98.9%; Score 2296.5; DB 2; Length 426;

Best Local Similarity 99.3%; Pred. No. 2.2e-217;

Matches 424; Conservative 0; Mismatches 2; Indels 1; Gaps 1;

Qy 1 MEWPARLCGLWALLLCAGGGGGGGGAAPTETQPPVTNLSVSVENLCTVIWTWNPPEGASS 60

|||||

Db 1 MEWPARLCGLWALLLCAGGGGGGGG-APTETQPPVTNLSVSVENLCTVIWTWNPPEGASS 59

Qy	61	NCSLWYFSHFSGDKQDKKIAPETRRSIEVPLNERICLQVGSQCSTNESEKPSILVEKCISP	120
Db	60	NCSLWYFSHFSGDKQDKKIAPETRRSIEVPLNERICLQVGSQCSTNESEKPSILVEKCISP	119
Qy	121	PEGDPESAVIELQCIWHNLSYMKCSWLPGRNTSPDTNYTLYYWHRSLEKIHQCENIFREG	180
Db	120	PEGDPESAVTELQCIWHNLSYMKCSWLPGRNTSPDTNYTLYYWHRSLEKIHQCENIFREG	179
Qy	181	QYFGCSFDLTKVKDSSFEQHSVQIMVKDNAGKIKPSFNIVPLTSRVKPDPPHIKNLSFHN	240
Db	180	QYFGCSFDLTKVKDSSFEQHSVQIMVKDNAGKIKPSFNIVPLTSRVKPDPPHIKNLSFHN	239
Qy	241	DDLIVQWENPQNFISRCLFYEVEVNNSQTETHNVFYVQEAKCENPEFERNVENTSCFMVP	300
Db	240	DDLIVQWENPQNFISRCLFYEVEVNNSQTETHNVFYVQEAKCENPEFERNVENTSCFMVP	299
Qy	301	GVLPTDLNTVRI RVKTNKLCYEDDKLWSNWSQEMSIGKKRNSTLYITMLLIVPVIVADAI	360
Db	300	GVLPTDLNTVRI RVKTNKLCYEDDKLWSNWSQEMSIGKKRNSTLYITMLLIVPVIVAGAI	359
Qy	361	IVLLLLYLKRLKIIIFPPIPDPGKIFKEMFGDQNDTDLHWKKYDIYEKQTKEETDSVVLIE	420
Db	360	IVLLLLYLKRLKIIIFPPIPDPGKIFKEMFGDQNDTDLHWKKYDIYEKQTKEETDSVVLIE	419
Qy	421	NLKKASQ 427	
Db	420	NLKKASQ 426	

US-09-688-286D-2

Qy 1 MEWPARLCGLWALLLCAGGGGGGGGAAPTETQPPVTNLSVSVENLCTVIWTWNPPEGASS 60

Art Unit: 1646

Db	1	MARPALLGELLVLLLT--ATVGQVAAATEVQPPVTNLSVSVENLCTIIWTWSPPEGASP	58
Qy	61	NCSLWYFSHFGDKQDKKIAPETRRSIEVPLNERICLVGSQCSTNESEKPSILVEKCISP	120
Db	59	NCTLRVYFSHFDDQDKKIAPETHRKEELPLDEKICLVGSQCSANESEKPSPLVKKCISP	118
Qy	121	PEGDPESAVIELQCIWHNLSYMKCSWLPGRNTSPDTNYTLYYWHRSLLEKIHCENIFREG	180
Db	119	PEGDPESAVTELKCIWHNLSYMKCSWLPGRNTSPDTHYTLYYWYSSLEKSRQCENIYREG	178
Qy	181	QYFGCSFDLTKVKDSSFEQHSVQIMVKDNAGKIKPSFNIVPLTSRVKPDPPHIKNLSFHN	240
Db	179	QHIACSFKLTKV-EPSFEHQNVQIMVKDNAGKIRPSCKIVSLTSYVKPDPPHIKHLKLN	237
Qy	241	DDLTVQWENPQNFISRCLFYEEVNNSTQETHNVFYVQEAKCENPEFERNVENTSCFMVP	300
Db	238	GALLVQWKNPQNFISRCLTYEEVNNSTQDRHNILEVEEDKCQNSESDRNMEGTSCFQLP	297
Qy	301	GVLPTDLNTVRIRVKTNKLCEYEDDKLWSNWSQEMSIGKKRNSTLYITMLLIVPVIVADAI	360
Db	298	GVLADAVYTVRVRVKTNKLCFDDNKLWSDWSEAQSIGKEQNSTFYTTMLLTIPVFVAVAV	357
Qy	361	IVLLLYLKRLKIIIFPPIPDGKIFKEMFGDQNDLTHWKKYDIYEKQTKETDSVVLIE	420
Db	358	IILFYLKRLKIIIFPPIPDGKIFKEMFGDQNDLTHWKKYDIYEKQSKEETDSVVLIE	417
Qy	421	NLKKAS	426
Db	418	NLKKAA	423

Wilson antibodies to NR4 (IL-13 receptor alpha) and its derivatives or its ligands (e.g. IL-13). Wilson further discloses such antibodies may be monoclonal or polyclonal and may be selected from naturally occurring antibodies to NR4 or may be specifically raised to NR4 or derivatives thereof. Antibodies to NR4 may be monoclonal or polyclonal (column 13). Alternatively, fragments of antibodies may be used such as Fab fragments, synthetic antibody that includes fragments and hybrid antibodies (i.e. single chain Fv) (column 14). Chemical coupling of fluorescent compounds such as fluorescein and rhodamine to antibodies (column 16).

Further, Wilson claims antibodies specifically:

**CLAIMS:**

1. An isolated antibody generated using an IL-13 receptor .alpha.-



Art Unit: 1646

chain polypeptide comprising all or part of SEQ ID NO: 4, which antibody binds to an IL-13 receptor .alpha.-chain.

2. An isolated antibody which binds specifically to an IL-13 receptor .alpha.-chain consisting of the sequence of SEQ ID NO: 4.

Therefore, because of the high homology between NR4 and SEQ ID NO:9

of instant application many of the antibodies disclosed by Wilson will specifically bind to the polypeptide of SEQ ID NO:9 of instant application. The disclosure of meets the limitation of claim 22-24, 26, 27, 29-35, absent evidence to the contrary.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

5. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Art Unit: 1646

Claim 22-37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Aman (see IDS, J. Biol. Chem., Vol. 271, No.46, November 15, pages 29265-29270, 1996) in view of Queen et al (5,693,762), Takatsu et al (US Patent 5,453,491) and Ladner (US Patent 4,946,778).

Aman discloses a polypeptide (IL-13 receptor alpha chain) which has 99.5% query match with the polypeptide of SEQ ID NO:9.

Sequence comparison of the Aman polypeptide and SEQ ID NO:9 of instant application is disclosed below:

## RESULT 1

I13R1\_HUMAN

ID I13R1\_HUMAN STANDARD; PRT; 427 AA.

AC P78552; O95646; Q99656;

DT 01-NOV-1997, integrated into UniProtKB/Swiss-Prot.

DT 01-MAY-1997, sequence version 1.

;

Query Match 99.5%; Score 2311; DB 1; Length 427;  
Best Local Similarity 99.5%; Pred. No. 6.2e-168;  
Matches 425; Conservative 0; Mismatches 2; Indels 0; Gaps 0;

Qy	1	MEWPARLCGLWALLLCAGGGGGGGAAPTETQPPVTNLSVSVENLCTVIWTWNPPEGASS	60
Db	1	MEWPARLCGLWALLLCAGGGGGGGAAPTETQPPVTNLSVSVENLCTVIWTWNPPEGASS	60
Qy	61	NCSLWYFSHFQDKQDKKIAPETRRSIEVPLNERICLQVGSQCSTNESEKPSILVEKCISP	120
Db	61	NCSLWYFSHFQDKQDKKIAPETRRSIEVPLNERICLQVGSQCSTNESEKPSILVEKCISP	120
Qy	121	PEGDPESAVIELQCIWHNLSYMKCSWLPGRNTSPDTNYTLYYWHRSLEKIHQCENIFREG	180
Db	121	PEGDPESAVTELQCIWHNLSYMKCSWLPGRNTSPDTNYTLYYWHRSLEKIHQCENIFREG	180
Qy	181	QYFGCSFDLTQVVDSSFEQHSVQIMVKDNAGKIKPSFNIVPLTSRVKPDPPHIKNLSFHN	240
Db	181	QYFGCSFDLTQVVDSSFEQHSVQIMVKDNAGKIKPSFNIVPLTSRVKPDPPHIKNLSFHN	240
Qy	241	DDLQVQWENPQNFISRCLFYEEVNNSQTETHNVFYVQEAACENPEFERNVENTSCFMVP	300
Db	241	DDLQVQWENPQNFISRCLFYEEVNNSQTETHNVFYVQEAACENPEFERNVENTSCFMVP	300
Qy	301	GVLPDTLNTVRIRVKTNKLCEYEDDKLWSNWSQEMSIGKKRNSTLYITMLLIVPVIVADAI	360
Db	301	GVLPDTLNTVRIRVKTNKLCEYEDDKLWSNWSQEMSIGKKRNSTLYITMLLIVPVIVAGAI	360
Qy	361	IVLLLLYLKRLKIIIFPPIPDGPKIFKEMFGDQNDTLHWKKYDIYEKQTKETDSVVLIE	420
Db	361	IVLLLLYLKRLKIIIFPPIPDGPKIFKEMFGDQNDTLHWKKYDIYEKQTKETDSVVLIE	420

Art Unit: 1646

Qy	421	NLKKASQ	427
Db	421	NLKKASQ	427

Aman does not teach isolated antibodies that bind IL-13 receptor alpha chain, but does disclose that the development of said antibodies may be useful in determining the binding of IL-4Ralpha and IL-13Ralpha (see page 29269 and 29265). Queen (5,693,762), teaches the production of humanized antibodies by using such molecules as IL-2 receptor (column 16), Fab fragments, (Fab')<sub>2</sub> and single chain antibodies (column 17). Antibodies in combination with pharmaceutical agents (column 19). Ladner discloses humanized antibodies are important because they bind to the same antigen as the original antibodies, but are less immunogenic when injected into humans.

Ladner (US Patent 4,946,778) discloses the production of single chain antibodies.

Takatsu discloses production of antibodies to IL-5. The production of antibodies to polypeptides is routine in the art and Takatsu is but one of the many examples available in the prior art. Takatsu discloses the production antibodies, e.g. those that inhibited the binding of IL-5 to IL-5R.

It would have been prima facie obvious to a person of ordinary skill in the art at the time the invention was made to use the polypeptide disclosed by Aman and use the method of Queen, Ladner and Takatsu to raise monoclonal, polyclonal, humanized antibodies and suspend them in pharmaceutically active agents and use them to bind to IL13 alpha receptor disclosed by Aman. It would have been prima facie obvious to a person of ordinary skill in the art at the time

Art Unit: 1646

the invention was made to use the polypeptide disclosed by Aman and use the method of Queen, Ladner and Takatsu to raise Fab fragments, (Fab')<sub>2</sub> and single chain antibodies (Fv) and suspend them in pharmaceutically active agents and use them to bind to IL13 alpha receptor disclosed by Aman. The ordinary artisan would have, been motivated to produce said antibody to study the interaction of IL4R alpha with IL-13R alpha. Antibodies to IL receptors have been routinely produced in the art with success.

The ordinary artisan would have expected success at producing said antibody because antibody production is a well defined art, using well-established techniques. Many of the antibodies produced by using the polypeptide of Aman would be expected to bind to the polypeptide of SEQ ID NO:9 of instant application due to the close homology of the two polypeptides, absent evidence to the contrary.

6. Claims 22-37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hilton (see Proc. Natl. Acad. Sci. USA. Vol. 93, pages 497-501, January 1996) in view of Aman (IDS, J. Biol. Chem., Vol. 271, No.46, November 15, pages 29265-29270, 1996) and Takatsu et al (US Patent 5,453,491), Queen et al (5,693,762) and Ladner (US Patent 4,946,778).

Hilton discloses a polypeptide (IL-13 receptor alpha chain), which has 72.9% query match with the polypeptide of SEQ ID NO:9.

Sequence comparison of the Hilton polypeptide and SEQ ID NO:9 of instant application is disclosed below:

RESULT 9  
I13R1\_MOUSE

Art Unit: 1646

ID I13R1\_MOUSE STANDARD; PRT; 424 AA.  
 AC O09030; Q7TT27;  
 DT 01-NOV-1997, integrated into UniProtKB/Swiss-Prot.  
 DT 01-JUL-1997, séquence version 1.

Query Match 72.9%; Score 1692.5; DB 1; Length 424;  
 Best Local Similarity 74.6%; Pred. No. 1.1e-120;  
 Matches 318; Conservative 40; Mismatches 65; Indels 3; Gaps 2;

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Qy      1 MEWPARLCGLWALLLCAGGGGGGGGAAPTETQPPVTNLSVSVENLCTVIWTWNPPEGASS 60
      | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
Db      1 MARPALLGELLVLLLT--ATVGQVAAATEVQPPVTNLSVSVENLCTIWTWSPPEGASP 58

Qy     61 NCSLWYFSHFGDKQDKKIAPETRRSIEVPLNERICLQVGSQCSTNESEKPSILVEKCIISP 120
      | | : | | | | | | | | | | | | | | | | | | | | | | | | | | | |
Db     59 NCTLRYFSHFDDQQDKKIAPETHRKEELPLDEKICLQVGSQCSANESKPSPLVKKCIISP 118

Qy    121 PEGDPESAVIELQCIWHNLSYMKCSWLPGRNTSPDTNYTLYYWHRSLEKIHQCENIFREG 180
      | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
Db    119 PEGDPESAVTELKCIWHNLSYMKCSWLPGRNTSPDTHYTLYYWYSSLEKSRQCENIYREG 178

Qy    181 QYFGCSFDLTQVKDSSFEQHSVQIMVKDNAGKIKPSFNIVPLTSRVKPDPPHIKNLSFHN 240
      | : | | | | | | | : | | | : | | | | | | | | | | | | | | | |
Db    179 QHIACSFKLTKV-EPSEHQNVQIMVKDNAGKIRPSCKIVSLTSYVKPDPPHIKHLKLN 237

Qy    241 DDLYVQWENPQNFI SRCLFYEEVNNSQTETHNVFYVQEAKCENPEFERNVENTSCFMVP 300
      | | | : | | | | | | | | | | | | | | | | | | | | | | | | | |
Db    238 GALLVQWKNPQNFRSRCLTYEEVNNTQTDRHNILEVEEDKCQNSESDRNMEGTSCFQLP 297

Qy    301 GVLPTLNTVIRIVKTNKLCYEDDKLWSNWSQEMSIGKKRNSTLYITMLLIVPVIVADAI 360
      | | | | : | | : | | | | | | | | | | | | | | | | | | | | |
Db    298 GVLADAVYTVRVRVKTNKLCFDDNKLWSDWSEAQSIGKEQNSTFYTTMLLTIPVFVAVAV 357

Qy    361 IVLLLYLKRLKIIIFPPIPDPGKIFKEMFGDQNDLTHWKKYDIYEKQTKETDSVVLIE 420
      | : | | | | | | | | | | | | | | | | | | | | | | | | | | | |
Db    358 IILFYLKRLKIIIFPPIPDPGKIFKEMFGDQNDLTHWKKYDIYEKQSKEETDSVVLIE 417

Qy    421 NLKKAS 426
      | | | | :
Db    418 NLKKAA 423
  
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Hilton discloses a NR4 polypeptide (IL-13 receptor) which binds IL-13 and together with IL-4R-alpha can form a functional receptor for IL-13 (see Fig 1, Abstract and Discussion). Hilton does not disclose isolated antibodies that bind (IL-13 receptor alpha chain)

Aman discloses that isolated antibodies that bind IL-13 receptor alpha may be useful in determining the binding of IL-4Ralpha and IL-13Ralpha (see page 29269 and 29265).

The teachings of Ladner, Queen and Takatsu are disclosed above.

It would have been prima facie obvious to a person of ordinary skill in the art at the time the invention was made to take the polypeptide disclosed by Hilton and by using the methods of Queen, Takatsu and Ladner raise antibodies that bind to IL13 alpha receptor disclosed by Hilton. The ordinary artisan would have been motivated to produce said antibody to study the interaction of IL4R alpha with IL-13R alpha as disclosed by Aman. Antibodies to IL receptors have been routinely produced in the art with success.

The ordinary artisan would have expected success at producing said antibody because antibody production is a well defined art using well established techniques. Many of the antibodies produced by using the polypeptide of Hilton would also be expected to bind to the polypeptide of SEQ ID NO:9 of instant application due to the close homology of the two polypeptides, absent evidence to the contrary.

It would have been prima facie obvious to a person of ordinary skill in the art at the time the invention was made to use the polypeptide disclosed by Hilton and use the method of Aman, Queen, Ladner and Takatsu to raise monoclonal, polyclonal, humanized and antibodies and suspend them in pharmaceutically active agents and use them to bind to IL13 alpha receptor disclosed by Hilton. It would have been prima facie obvious to a person of ordinary skill in the art at the time the invention was made to use the polypeptide disclosed by Aman and use the method of Queen, Ladner and Takatsu to raise Fab fragments, (Fab')<sub>2</sub> and single chain antibodies (Fv) and suspend them in pharmaceutically active agents and use them to bind to IL13 alpha receptor disclosed by Aman. The ordinary

Art Unit: 1646

artisan would have been motivated to produce said antibody to study the interaction of IL4R alpha with IL-13R alpha. The ordinary artisan would have expected success at producing said antibody because antibody production is a well defined art using well-established techniques. Many of the antibodies produced by using the polypeptide of Hilton would be expected to bind to the polypeptide of SEQ ID NO:9 of instant application due to the close homology of the two polypeptides, absent evidence to the contrary.

7. Claims 25 and 28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wilson (US Patent 6,911,530) in view of Queen et al (5,693,762).

Wilson discloses a method of making various antibodies that bind to NR4 polypeptide. The teachings of Wilson are disclosed below. The NR4 polypeptide (SEQ ID NO:4 and 2) of Wilson has 98.9% and 72.9% query match respectively, with the polypeptide of SEQ ID NO:9 of instant application (IL-13 receptor).

Wilson does not disclose humanized antibodies.

Queen (5,693,762), teaches the production of humanized antibodies by using such molecules as IL-2 receptor (column 16). Fab fragments, (Fab')<sub>2</sub> and single chain antibodies (column 17). Antibodies in combination with pharmaceutical agents (column 19). Ladner further discloses humanized antibodies are important because they bind to the same antigen as the original antibodies, but are less immunogenic when injected into humans.

Art Unit: 1646

It would have been prima facie obvious to a person of ordinary skill in the art at the time the invention was made to take the polypeptide disclosed by Wilson and by using the method of Queen to raise antibodies that bind to the NR4 (IL13 alpha receptor) The ordinary artisan would have been motivated to produce said antibody to study the interaction of IL4R alpha with IL-13R alpha as well as to use in human immunotherapy because humanized antibodies are important because they bind to the same antigen as the original antibodies, but are less immunogenic when injected into humans.

The ordinary artisan would have expected success at producing said antibody because humanized antibody production is a well defined art using well-established techniques. Many of the antibodies produced by using the polypeptide of Wilson would be expected to bind to the polypeptide of SEQ ID NO:9 of instant application due to the close homology of the two polypeptides, absent evidence to the contrary.

8. Claims 38-39 and 42-43 are allowable.

9. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is



Art Unit: 1646

filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Art Unit: 1646

Advisory

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nirmal S. Basi whose telephone number is 571-272-0868. The examiner can normally be reached on 9:00 AM-5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol can be reached on 571-272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Nirmal S. Basi  
Art Unit 1646

*N/S*

CHRISTINE J. SAOUD  
PRIMARY EXAMINER

*Christine J. Saoud*